

## **AMENDMENTS TO THE CLAIMS**

The following listing of claims replaces all prior claims in the subject application.

1-35. (Cancelled).

36. (New) A recombinant mutant *Bet v 1* allergen derived from a naturally-occurring *Bet v 1* allergen, said recombinant mutant *Bet v 1* allergen having:

- (a) a substitution of a solvent-accessible amino acid residue that is conserved among *Bet v 1* homologous allergens within the taxonomic order from which said naturally-occurring *Bet v 1* allergen originates, said substitution occurring in a B-cell epitope of said naturally-occurring *Bet v 1* allergen;
- (b) reduced specific IgE binding compared to said naturally-occurring *Bet v 1* allergen from which it is derived; and
- (c) an  $\alpha$ -carbon backbone tertiary structure that is preserved as compared to the  $\alpha$ -carbon backbone tertiary structure of said naturally-occurring *Bet v 1* allergen.

37. (New) The recombinant mutant *Bet v 1* allergen of claim 36 which comprises one or more amino acid substitutions selected from the group consisting of:

- (i) Pro at position 10 of SEQ ID NO: 37;
- (ii) Gly at position 25 of SEQ ID NO: 37;
- (iii) Thr at position 28 of SEQ ID NO: 37, and Gln at position 32 of SEQ ID NO: 37;
- (iv) Ser at position 45 of SEQ ID NO: 37;
- (v) Ser at position 47 of SEQ ID NO: 37;
- (vi) Asn at position 55 of SEQ ID NO: 37;
- (vii) Ala at position 77 of SEQ ID NO: 37;
- (viii) Gly at position 108 of SEQ ID NO: 37; and
- (ix) Thr at position 28 of SEQ ID NO: 37, Gln at position 32 of SEQ ID NO: 37, Ser at position 45 of SEQ ID NO: 37, and Gly at position 108 of SEQ ID NO: 37.

38. (New) The recombinant mutant *Bet v 1* allergen of claim 36, wherein said solvent-accessible conserved amino acid residue has a solvent accessibility of at least 20%.

39. (New) The recombinant mutant *Bet v 1* allergen of claim 36, wherein said conserved solvent-accessible amino acid residue is conserved with more than 70% identity among *Bet v 1* homologous allergens within the taxonomic order from which said naturally-occurring *Bet v 1* allergen originates.

40. (New) The recombinant mutant *Bet v 1* allergen of claim 36, wherein the specific IgE binding of said mutant *Bet v 1* allergen compared to said naturally-occurring *Bet v 1* allergen from which it is derived is reduced by at least 5%.

41. (New) The recombinant mutant *Bet v 1* allergen of claim 36, wherein the average root mean square deviation of the atomic coordinates comparing the  $\alpha$ -carbon backbone tertiary structures of said recombinant mutant *Bet v 1* allergen and said naturally-occurring *Bet v 1* allergen is less than 2 $\text{\AA}$ .

42. (New) The recombinant mutant *Bet v 1* allergen of claim 36, wherein said conserved solvent-accessible amino acid residue is within a patch of conserved amino acid residues connected over at least 400 $\text{\AA}$  of the surface of said naturally-occurring *Bet v 1* allergen.

43. (New) The recombinant mutant *Bet v 1* allergen of claim 36, wherein said solvent-accessible amino acid residue that is conserved among *Bet v 1* homologous allergens within the taxonomic order from which said naturally-occurring *Bet v 1* allergen is substituted with an amino acid that is not conserved among *Bet v 1* homologous allergens within the taxonomic order from which said naturally-occurring *Bet v 1* allergen occurs.

44. (New) A recombinant mutant *Ves v 5* allergen derived from a naturally-occurring *Ves v 5* allergen, said recombinant mutant *Ves v 5* allergen having:

(a) a substitution of a solvent-accessible amino acid residue that is conserved among *Ves v 5* homologous allergens within the taxonomic order from which said naturally-

occurring *Ves v 5* allergen originates, said substitution occurring in a B-cell epitope of said naturally-occurring *Ves v 5* allergen;

(b) having reduced specific IgE binding compared to said naturally-occurring *Ves v 5* allergen from which it is derived; and

(c) an  $\alpha$ -carbon backbone tertiary structure that is preserved as compared to the  $\alpha$ -carbon backbone tertiary structure of said naturally-occurring *Ves v 5* allergen.

45. (New) The recombinant mutant *Ves v 5* allergen of claim 44 which comprises one or more amino acid substitutions selected from the group consisting of:

- i) Ala at position 72 of SEQ ID NO: 39; and
- ii) Ala at position 96 of SEQ ID NO: 39.

46. (New) The recombinant mutant *Ves v 5* allergen of claim 44, wherein said solvent-accessible conserved amino acid residue has a solvent accessibility of at least 20%.

47. (New) The recombinant mutant *Ves v 5* allergen of claim 44, wherein said conserved solvent-accessible amino acid residue is conserved with more than 70% identity among *Ves v 5* homologous allergens within the taxonomic order from which said naturally-occurring *Ves v 5* allergen originates.

48. (New) The recombinant mutant *Ves v 5* allergen of claim 44, wherein the specific IgE binding of said mutant *Ves v 5* allergen compared to said naturally-occurring *Ves v 5* allergen from which it is derived is reduced by at least 5%.

49. (New) The recombinant mutant *Ves v 5* allergen of claim 44, wherein the average root mean square deviation of the atomic coordinates comparing the  $\alpha$ -carbon backbone tertiary structures of said recombinant mutant *Ves v 5* allergen and said naturally-occurring *Ves v 5* allergen is less than 2 $\text{\AA}$ .

50. (New) The recombinant mutant *Ves v 5* allergen of claim 44, wherein said conserved solvent-accessible amino acid residue is within a patch of conserved amino acid residues connected over at least 400Å of the surface of said naturally-occurring *Ves v 5* allergen.

51. (New) The recombinant mutant *Ves v 5* allergen of claim 44, wherein said solvent-accessible amino acid residue that is conserved among *Ves v 5* homologous allergens within the taxonomic order from which said naturally-occurring *Ves v 5* allergen is substituted with an amino acid that is not conserved among *Ves v 1* homologous allergens within the taxonomic order from which said naturally-occurring *Ves v 5* allergen occurs.

52. (New) A method of preparing a recombinant mutant *Bet v 1* allergen, which method comprises:

identifying an amino acid residue in a B-cell epitope of a naturally-occurring *Bet v 1* allergen that is conserved among homologous *Bet v 1* proteins within the taxonomic order from which said naturally-occurring *Bet v 1* allergen originates; and

substituting said identified amino acid residue to form a mutant *Bet v 1* allergen.

53. (New) The method of claim 52 further comprising determining that the α-carbon backbone tertiary structure of said mutant *Bet v 1* allergen is preserved compared with the α-carbon backbone tertiary structure of said naturally-occurring *Bet v 1* allergen.

54. (New) The method of claim 52 further comprising determining that said mutant *Bet v 1* allergen has reduced specific IgE binding compared to said naturally-occurring *Bet v 1* allergen.

55. (New) The method of claim 52, wherein said substituted conserved amino acid residue has a solvent accessibility of at least 20%.

56. (New) The method of claim 52, wherein said substituted amino acid residue is conserved with more than 70% identity among *Bet v 1* homologous allergens within the taxonomic order from which said naturally-occurring *Bet v 1* allergen originates.

57. (New) The method of claim 52 wherein said identified amino acid is within a conserved patch connected over at least 400 Å<sup>2</sup> of the surface of the three-dimensional structure of said naturally-occurring *Bet v 1* allergen.

58. (New) The method of claim 52 which comprises substituting said identified amino acid residue with an amino acid that is not conserved among *Bet v 1* homologous allergens within the taxonomic order from which said naturally-occurring *Bet v 1* allergen occurs.

59. (New) A method of preparing a recombinant mutant *Ves v 5* allergen, which method comprises:

identifying an amino acid residue in a B-cell epitope of a naturally-occurring *Ves v 5* allergen that is conserved among homologous *Ves v 5* proteins within the taxonomic order from which said naturally-occurring *Ves v 5* allergen originates; and  
substituting said identified amino acid residue to form a mutant *Ves v 5* allergen.

60. (New) The method of claim 59 further comprising determining that the α-carbon backbone tertiary structure of said mutant *Ves v 5* allergen is preserved compared with the α-carbon backbone tertiary structure of said naturally-occurring *Ves v 5* allergen.

61. (New) The method of claim 59 further comprising determining that said mutant *Ves v 5* allergen has reduced specific IgE binding compared to said naturally-occurring *Ves v 5* allergen.

62. (New) The method of claim 59, wherein said substituted conserved amino acid residue has a solvent accessibility of at least 20%.

63. (New) The method of claim 59, wherein said substituted amino acid residue is conserved with more than 70% identity among *Ves v 5* homologous allergens within the taxonomic order from which said naturally-occurring *Ves v 5* allergen originates.

64. (New) The method of claim 59 wherein said identified amino acid is within a conserved patch connected over at least 400 Å<sup>2</sup> of the surface of the three-dimensional structure of said naturally-occurring *Ves v 5* allergen.

65. (New) The method of claim 59 which comprises substituting said identified amino acid residue with an amino acid that is not conserved among *Ves v 5* homologous allergens within the taxonomic order from which said naturally-occurring *Ves v 5* allergen occurs.

66. (New) A recombinant mutant allergen derived from a naturally-occurring allergen selected from the group consisting of (i) allergens homologous to *Bet v 1*; and (ii) vespid antigen 5 allergens,

said recombinant mutant allergen having:

(a) a substitution of a solvent-accessible amino acid residue that is conserved among homologous allergens within the taxonomic order from which said naturally-occurring allergen originates, said substitution occurring in a B-cell epitope of said naturally-occurring allergen;

(b) reduced specific IgE binding compared to said naturally-occurring allergen; and

(c) an α-carbon backbone tertiary structure that is preserved as compared to the α-carbon backbone tertiary structure of said naturally-occurring allergen.

67. (New) The recombinant allergen according to claim 66 wherein said allergens homologous to *Bet v 1* have an amino sequence that yields a BLAST probability of less than 0.1 when compared to an amino acid sequence of SEQ ID NO: 37.

68. (New) The recombinant mutant allergen of claim 66, wherein said solvent-accessible conserved amino acid residue has a solvent accessibility of at least 20%.

69. (New) The recombinant mutant allergen of claim 66, wherein said conserved solvent-accessible amino acid residue is conserved with more than 70% identity among homologous allergens within the taxonomic order from which said naturally-occurring allergen originates.

70. (New) The recombinant mutant allergen of claim 66, wherein the specific IgE binding of said mutant allergen compared to said naturally-occurring allergen from which it is derived is reduced by at least 5%.

71. (New) The recombinant mutant allergen of claim 66, wherein the average root mean square deviation of the atomic coordinates comparing the  $\alpha$ -carbon backbone tertiary structures of said recombinant mutant allergen and said naturally-occurring allergen is less than 2 $\text{\AA}$ .

72. (New) The recombinant mutant allergen of claim 66, wherein said conserved solvent-accessible amino acid residue is within a patch of conserved amino acid residues connected over at least 400 $\text{\AA}^2$  of the surface of said naturally-occurring allergen.

73. (New) The recombinant mutant allergen of claim 66, wherein said solvent-accessible amino acid residue that is conserved among homologous allergens within the taxonomic order from which said naturally-occurring allergen is substituted with an amino acid that is not conserved among homologous allergens within the taxonomic order from which said naturally-occurring allergen occurs.

74. (New) A method of preparing a recombinant mutant allergen derived from a naturally-occurring allergen selected from the group consisting of (i) allergens homologous to *Bet v 1*; and (ii) vespid antigen 5 allergens, which method comprises:

identifying an amino acid residue in a B-cell epitope of said naturally-occurring allergen that is conserved among homologous proteins within the taxonomic order from which said naturally-occurring allergen originates; and

substituting said identified amino acid residue to form a mutant allergen.

75. (New) The method of claim 74 wherein said allergens homologous to *Bet v 1* have an amino sequence that yields a BLAST probability of less than 0.1 when compared to an amino acid sequence of SEQ ID NO: 37.

76. (New) The method of claim 74 further comprising determining that the  $\alpha$ -carbon backbone tertiary structure of said mutant allergen is preserved compared with the  $\alpha$ -carbon backbone tertiary structure of said naturally-occurring allergen.

77. (New) The method of claim 74 further comprising determining that said mutant allergen has reduced specific IgE binding compared to said naturally-occurring allergen.

78. (New) The method of claim 74, wherein said substituted conserved amino acid residue has a solvent accessibility of at least 20%.

79. (New) The method of claim 74, wherein said substituted amino acid residue is conserved with more than 70% identity among homologous allergens within the taxonomic order from which said naturally-occurring allergen originates.

80. (New) The method of claim 74 wherein said identified amino acid is within a conserved patch connected over at least 400  $\text{\AA}^2$  of the surface of the three-dimensional structure of said naturally-occurring allergen.

81. (New) The method of claim 74 which comprises substituting said identified amino acid residue with an amino acid that is not conserved among homologous allergens within the taxonomic order from which said naturally-occurring allergen occurs.

82. (New) A recombinant mutant allergen derived from a naturally-occurring allergen, said recombinant mutant allergen having:

- (a) a substitution of a solvent-accessible amino acid residue that is conserved among homologous allergens within the taxonomic order from which said naturally-occurring allergen originates, said substitution occurring in a B-cell epitope of said naturally-occurring allergen;
- (b) reduced specific IgE binding compared to said naturally-occurring allergen from which it is derived; and
- (c) an  $\alpha$ -carbon backbone tertiary structure that is preserved as compared to the  $\alpha$ -carbon backbone tertiary structure of said naturally-occurring allergen.

83. (New) The recombinant mutant allergen of claim 82, wherein said solvent-accessible conserved amino acid residue has a solvent accessibility of at least 20%.

84. (New) The recombinant mutant allergen of claim 82, wherein said conserved solvent-accessible amino acid residue is conserved with more than 70% identity among homologous allergens within the taxonomic order from which said naturally-occurring allergen originates.

85. (New) The recombinant mutant allergen of claim 82, wherein the specific IgE binding of said mutant allergen compared to said naturally-occurring allergen from which it is derived is reduced by at least 5%.

86. (New) The recombinant mutant allergen of claim 82, wherein the average root mean square deviation of the atomic coordinates comparing the  $\alpha$ -carbon backbone tertiary structures of said recombinant mutant allergen and said naturally-occurring allergen is less than 2 $\text{\AA}$ .

87. (New) The recombinant mutant allergen of claim 82, wherein said conserved solvent-accessible amino acid residue is within a patch of conserved amino acid residues connected over at least 400 $\text{\AA}^2$  of the surface of said naturally-occurring allergen.

88. (New) The recombinant mutant allergen of claim 82, wherein said solvent-accessible amino acid residue that is conserved among homologous allergens within the taxonomic order from which said naturally-occurring allergen occurs is substituted with an amino acid that is not conserved among homologous allergens within the taxonomic order from which said naturally-occurring allergen occurs.

89. (New) A method of preparing a recombinant mutant allergen comprising, identifying an amino acid residue in a B-cell epitope of a naturally-occurring allergen that is conserved among homologous proteins within the taxonomic order from which said naturally-occurring allergen originates; and substituting said identified amino acid residue to form a mutant allergen.

90. (New) The method of claim 89 further comprising determining that the  $\alpha$ -carbon backbone tertiary structure of said mutant allergen is preserved compared with the  $\alpha$ -carbon backbone tertiary structure of said naturally-occurring allergen.

91. (New) The method of claim 89 further comprising determining that said mutant allergen has reduced specific IgE binding compared to said naturally-occurring allergen.

92. (New) The method of claim 89, wherein said substituted conserved amino acid residue has a solvent accessibility of at least 20%.

93. (New) The method of claim 89, wherein said substituted amino acid residue is conserved with more than 70% identity among homologous allergens within the taxonomic order from which said naturally-occurring allergen originates.

94. (New) The method of claim 89 wherein said identified amino acid is within a conserved patch connected over at least 400  $\text{\AA}^2$  of the surface of the three-dimensional structure of said naturally-occurring allergen.

95. (New) The method of claim 89 which comprises substituting said identified amino acid residue with an amino acid that is not conserved among homologous allergens within the taxonomic order from which said naturally-occurring allergen occurs.

96. (New) A method for preparing a recombinant mutant allergen, which method comprises expressing a recombinant construct encoding a naturally occurring allergen in which an amino acid residue in a B-cell epitope of a naturally occurring allergen that is conserved among said naturally occurring allergen and homologous proteins within the taxonomic order from which said naturally occurring allergen originated has been substituted; and purifying said mutant allergen.